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Predictors of pacing-dependency in patients with cardiovascular implantable electronic devices

Running title: Predictors of pacing-dependency

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Abstract

Background: Data on the prevalence and predictors for the development of pacing-dependency in patients with cardiovascular implantable electronic devices (CIEDs) are sparse.

Methods: Pacing-dependency defined as an absence of intrinsic rhythm of ≥ 30 bpm was determined in 802 consecutive patients with CIEDs who visited the documented pacemaker or implantable cardioverter-defibrillator outpatient clinic for routine follow-up.

Results: A total of 131 (16%) patients were found to be pacing-dependent 67 ± 70 months after CIED implant. Multivariate analysis revealed a significant association between pacing-dependency and the following clinical variables: second or third-degree atrioventricular (AV) block at implant (OR = 19.9; 95% CI: 10.9–38.5, $p < 0.01$), atrial fibrillation at implant (OR = 2.15; 95% CI: 1.16–4.05, $p = 0.02$), left ventricular ejection fraction (LVEF) $\leq 30\%$ (OR = 2.06; 95% CI: 1.03–4.15, $p = 0.04$), brain natriuretic peptide (BNP) > 150 pg/mL (OR = 2.12; 95% CI: 1.16–3.97, $p = 0.02$), chronic kidney disease (OR = 1.86; 95% CI: 1.08–3.26, $p = 0.03$), and during follow-up after implantation > 5 years (OR = 3.29; 95% CI: 1.96–5.64, $p < 0.01$). None of the remaining clinical variables including age, gender, diabetes mellitus, underlying heart disease, prior cardiac surgery or medication during follow-up including beta-blockers and amiodarone predicted pacing-dependency.

Conclusions: Pacing-dependency is associated with second or third-degree AV-block at implant, atrial fibrillation before implant, low LVEF, elevated BNP, chronic kidney disease and during follow-up after implant.

Key words: pacing-dependency, permanent pacemaker, implantable cardioverter-defibrillator

Introduction

Knowledge of pacing-dependency following implantation of cardiovascular implantable electronic devices (CIEDs) is very important in various clinical settings including elective generator change, potential electromagnetic interference and management of suspected lead or generator malfunction [1, 2]. Although several million permanent pacemakers and implantable cardioverter-defibrillators (ICDs) with bradycardia pacing capability have been implanted 60 years after the first pacemaker implantation in 1958, few studies have investigated the prevalence of pacing dependency and clinical predictors for the development of pacing dependency [3–17]. Thus, the aim herein was to determine prevalence and predictors of pacing dependency in a well-defined cohort of 802 patients with pacemakers or implantable cardioverter-defibrillators at the documented clinic.

Methods

Study population

After written informed consent had been obtained, pacing dependency was determined prospectively in 802 consecutive patients who came to the pacemaker and ICD outpatient clinic for routine follow-up between January 2018 and December 2018 and in whom a permanent pacemaker or ICD had been implanted for at least 6 months by this institution. Pacing dependency was defined as an absence of intrinsic rhythm ≥ 30 bpm after lowering the pacing rate to 30 bpm for at least 10 s or after transient inhibition of pacing therapy (Fig. 1). A high-degree atrioventricular (AV) block at implant was defined as second degree AV block type Mobitz or third-degree AV block. Chronic kidney disease (CKD) of at least stage 3 was diagnosed in the presence of at least two estimated glomerular filtration rates (eGFR) using the Modification of Diet in Renal Disease formula below 60 mL/min per 1.73 m² with an interval of at least 3 months. The study protocol was reviewed and approved by the ethics committee of the Philipps-University of Marburg.

Statistical analysis

Results are expressed as mean \pm standard deviation (SD) for continuous variables with normal distribution and median values with interquartile range (IQR) for continuous variables without normal distribution. Univariate comparisons of clinical characteristics between patients

with and without pacing dependency were performed using the Student t-test or the Mann-Whitney U test for continuous variables, categorical values were compared using χ^2 and the Fisher exact tests, where appropriate. Logistic regression analysis was used to generate a multivariate model including all potential predictors of pacing dependency listed in Table 1 in order to investigate which factors showed independent effects on the risk of developing pacemaker dependency after adjustment for confounding by other factors including the presence or absence of ICD therapy as well as cardiac resynchronization therapy (CRT). All probability values reported are two-sided, and a probability value of $p < 0.05$ was considered to indicate statistical significance. R-software version 3.5.0 (www.R-project.org) was used for statistical analyses.

Results

Clinical characteristics

The clinical characteristics of 802 study patients are summarized in Table 1 and included 563 (70%) patients with a permanent pacemaker and 239 (30%) patients with an ICD. Mean duration between device implant and follow-up visit was 67 ± 70 months with a minimum implant duration of 6 months. The majority of patients were male (65%). Mean age at device implant was 74 ± 13 years. Indication for pacemaker implantation was a high-degree AV block in 247 (31%) patients, sick sinus syndrome in 196 (24%) patients, carotid sinus syndrome in 2 (0.2%) patients, and atrial fibrillation with bradycardia in 125 (16%) patients. CRT devices were implanted in 93 of 802 study patients (12%) including CRT pacemakers in 25 of 563 pacemaker patients (4%) and CRT defibrillators in 68 of 239 (28%) patients with an ICD.

Prevalence and predictors of pacing dependency

A total of 131 of 802 study patients (16%) were found to be pacing dependent at follow-up 67 ± 70 months after the device implant. Pacing dependency at follow-up was found significantly more often in patients with New York Heart Association (NYHA) heart failure class 3 or 4, elevated B-type natriuretic peptide (BNP) > 150 pg/mL, decreased left ventricular ejection fraction (LVEF) $\leq 30\%$, CKD, high degree AV block at implant, left bundle branch block on electrocardiogram at implant, and implant duration > 5 years (Table 1). Multivariate logistic regression analysis revealed a significant association between pacing dependency and the following 6 clinical variables: second or third-degree AV block at implant (odds ratio [OR] = 19.9; 95% confidence interval [CI]: 10.9–38.5, $p < 0.01$), atrial fibrillation at implant (OR = 2.15; 95% CI: 1.16–4.05, $p = 0.02$), LVEF $\leq 30\%$ (OR = 2.06; 95% CI: 1.03–4.15, $p = 0.04$), BNP > 150 pg/mL (OR = 2.12; 95% CI: 1.16–3.97, $p = 0.02$), CKD (OR = 1.86; 95% CI = 1.08–

3.26, $p = 0.03$), and follow-up duration > 5 years ($OR = 3.29$; 95% CI: 1.96–5.64, $p < 0.01$) (Table 2). None of the remaining clinical variables including age, gender, body mass index, arterial hypertension, diabetes mellitus, underlying heart disease, prior cardiac surgery, transcatheter aortic valve replacement or medication during follow-up including beta-blockers and amiodarone predicted pacing dependency.

Subgroup analysis of 563 patients with permanent pacemaker

The results for the subgroup of 563 patients with permanent pacemaker without cardioverter defibrillator back-up are summarized in Table 3. Pacing dependency at follow-up was found significantly more often in patients with NYHA heart failure class 3 or 4, elevated $BNP > 150$ pg/mL, decreased $LVEF \leq 30\%$, CKD, second or third-degree AV block at implant, and implant duration > 5 years.

Subgroup analysis of 239 patients with ICD

The results for the subgroup of 239 patients with ICD are summarized in Table 4. Pacing dependency at follow-up was found significantly more often in patients with NYHA heart failure class 3 or 4, elevated $BNP > 150$ pg/mL, decreased $LVEF \leq 30\%$, CKD, non-ischemic dilated cardiomyopathy, amiodarone therapy, and implant duration > 5 years. In addition, left bundle branch block at implant, which was treated with a CRT defibrillator in 68 patients with ICD, was also associated with a higher prevalence of pacing dependency at follow-up (Table 4).

Discussion

The main finding of the present study is a 16% prevalence of pacing dependency at 67 months mean follow-up, which was associated with second or third-degree AV-block at implant, atrial fibrillation before implant, low LVEF, elevated BNP, CKD and implant duration. Although it is generally accepted that pacing dependency means absence of a sufficient intrinsic rhythm resulting in bradycardia-related symptoms during inhibition of pacing, the definition of pacing dependency is still controversial [12–14]. Similar to previous studies [5–7, 10], the current study defined pacing dependency as absence of an intrinsic rhythm of at least 30 bpm during pacemaker inhibition or ventricular pacing at a rate of lower than 30 bpm, whereas other investigators used an upper rate cutoff for the intrinsic rhythm of 40 bpm [4, 8, 9, 11] or 50 bpm [3] to define pacing dependency. The observed prevalence of pacing dependency of 16% in the present study is similar to the prevalence of 22% in a relatively large Canadian Trial of Physiologic Pacing (CTOPP), in which a pacemaker dependency test was performed in 2244

patients [4]. Of note, the prevalence of pacing dependency varies in the literature between 2% in the study of Lekalowski et al. [6] and 63% in the study of Merin et al. [8] as summarized in Table 5. The discrepancy between these studies may, in part, be explained by differences in study patients as well as different definitions used for pacing dependency. Whereas the current study enrolled consecutive patients who came for routine device follow-up visits at the pacemaker and ICD outpatient department, Nagatamo et al. [5] excluded patients with an intrinsic rate of < 30 bpm at implant which likely contributed to a low prevalence of pacing dependency of 4% in the study by Nagatamo et al. [5]. In contrast to the study by Nagatamo et al. [5] and the present study, Merin et al. [8] found a high prevalence of pacing dependency of 63% during follow-up. This discrepancy is likely to be due to the fact that the majority of patients in the study of Merin et al. [8] received a permanent pacemaker for third degree AV block without sufficient ventricular escape rhythm following cardiac surgery [8].

The most important predictor of pacing dependency during follow-up in the current study was the presence second degree AV block type Mobitz or third-degree AV block at the time of pacemaker implant. This is consistent with the findings of most previous studies in patients with and without cardiac surgery prior to pacemaker implant [3, 5–8, 15–17]. Several previous investigators also found an association between pacing dependency during follow-up and body mass index [7], age [11], male gender [11], and a history of coronary artery disease [16]. Whereas none of these variables predicted pacing dependency in the present study, a significant association was found between pacing dependency and heart failure severity as indexed by a low LVEF \leq 30% and an elevated BNP level. Furthermore, amiodarone use was associated with pacing dependency in the subgroup of patients with ICD in the current study. This is consistent with the results of Sood et al. [11], who also found a significant association between pacing dependency and amiodarone use in a large cohort of 1058 patients with ICD. The results of the present study support the hypothesis that patients with heart failure and high degree AV block at implant will probably be paced more frequently in the ventricle and may therefore benefit from physiological pacing [4]. Although chronic kidney disease is a generally accepted important comorbidity in patients with heart disease of any etiology with regard to overall survival, the association between CKD and pacing dependency has not been investigated in previous studies [2–17]. Multivariate analysis in the current study revealed a twofold risk for pacing dependency in patients with CKD compared to patients without CKD.

Limitations of the study

There are several limitations of the present study. First, clinical patient data and implant data were collected retrospectively, although pacing dependency was determined prospectively

between January 2018 and December 2018 at the documented pacemaker and ICD outpatient department. Secondly, pacing dependency was determined during a brief period of time at a single outpatient visit. It is well known that pacing dependency can occur transiently. Therefore, repeated pacing dependency tests and longer monitoring time may have revealed patients, in whom pacing dependency may have resolved or may have occurred at other times.

Conclusions

In conclusion, pacing dependency after CIED implantation depends on the pacing indication and is much more common in patients with high-degree AV-block at implant compared to patients with sick sinus syndrome. In addition, pacing dependency is associated with more advanced heart failure, chronic kidney disease and follow-up duration after implant. Since pacing dependent patients who suffer from heart failure will need frequent ventricular pacing, physiological pacing should be considered in these patients.

Conflict of interest: None declared

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Table 1. Clinical characteristics of 802 patients with and without pacing dependency.

| | All patients | Pacing-dependency | | P |
|--|--------------|-------------------|--------------|--------|
| Clinical variable | N = 802 | Yes (n = 131) | No (n = 671) | |
| Age [years] | 74 ± 13 | 75 ± 12 | 74 ± 13 | 0.23 |
| Male gender | 521 (65%) | 89 (68%) | 432 (64%) | 0.50 |
| Body mass index [kg/m ²] | 28 ± 12 | 28 ± 5 | 28 ± 13 | 0.86 |
| Arterial hypertension | 622 (78%) | 105 (80%) | 517 (77%) | 0.27 |
| Diabetes mellitus | 143 (18%) | 19 (15%) | 124 (18%) | 0.43 |
| Atrial fibrillation before implant | 242 (30%) | 38 (29%) | 205 (31%) | 0.78 |
| Left bundle branch block at implant | 141 (18%) | 25 (19%) | 116 (17%) | 0.62 |
| Chronic kidney disease | 330 (41%) | 70 (53%) | 260 (39%) | < 0.01 |
| Heart failure severity | | | | |
| Left ventricular ejection fraction ≤ 30% | 179 (22%) | 41 (31%) | 138 (21%) | < 0.01 |

| | | | | |
|--|------------|---------------|------------|--------|
| NYHA functional class III or IV | 320 (40%) | 74 (56%) | 246 (37%) | < 0.01 |
| B-type natriuretic peptide >150 pg/mL ^a | 408 (57%) | 77 (71%) | 331 (54%) | < 0.01 |
| Underlying cardiac disease | | | | |
| Coronary artery disease | 313 (39%) | 45 (34%) | 268 (40%) | 0.07 |
| Nonischemic dilated cardiomyopathy | 119 (15%) | 26 (20%) | 93 (14%) | |
| Hypertensive heart disease | 180 (22%) | 35 (31%) | 145 (22%) | |
| Valvular heart disease | 101 (13%) | 17 (15%) | 84 (13%) | |
| Other cardiac diseases ^b | 13 (2%) | 4 (4%) | 9 (1%) | |
| No structural heart disease | 76 (9%) | 4 (4%) | 72 (11%) | |
| Previous cardiac surgery | | | | |
| Aortocoronary bypass grafting | 95 (12%) | 17 (13%) | 78 (12%) | 0.77 |
| Surgical aortic valve replacement | 29 (4%) | 4 (3%) | 25 (4%) | 0.90 |
| Mitral valve reconstruction or replacement | 15 (2%) | 1 (1%) | 14 (2%) | 0.50 |
| Transcatheter aortic valve replacement | 43 (5%) | 9 (7%) | 34 (5%) | 0.53 |
| Cardiovascular implantable electronic device | | | | |
| Antibradycardia pacemaker | 563 (70%) | 103 (79%) | 460 (69%) | 0.02 |
| Implantable cardioverter-defibrillator | 239 (30%) | 28 (21%) | 211 (31%) | |
| Cardiac resynchronization therapy device | 93 (12%) | 20 (15%) | 73 (11%) | 0.07 |
| Median amount of ventricular pacing (IQR) | 30% (1–99) | 100% (99–100) | 12% (1–82) | < 0.01 |
| Indication for CIED implantation | | | | |
| Sick sinus syndrome | 196 (24%) | 12 (9%) | 184 (27%) | < 0.01 |
| Second or third-degree AV block | 247 (31%) | 95 (73%) | 152 (23%) | |
| Atrial fibrillation with bradycardia | 125 (16%) | 14(11%) | 111 (17%) | |
| Carotid sinus syndrome | 2 (0.2%) | 0 (0%) | 2 (0.3%) | |
| Prophylactic ^c | 232 (29%) | 10 (7%) | 222 (33%) | |
| Implant duration > 5 years | 330 (41%) | 74 (56%) | 256 (38%) | < 0.01 |
| Medication | | | | |
| Beta-blockers | 539 (67%) | 85 (65%) | 454 (68%) | 0.14 |
| Amiodarone | 44 (5%) | 7 (5%) | 37 (6%) | 0.94 |
| Digitalis | 68 (8%) | 9 (7%) | 59 (9%) | 0.58 |
| ACEI | 419 (52%) | 77 (59%) | 342 (51%) | 0.12 |
| Angiotensin receptor blockers | 171 (21%) | 25 (19%) | 146 (22%) | 0.57 |
| Diuretics | 549 (68%) | 100 (76%) | 449 (67%) | 0.04 |

| | | | | |
|----------------------------------|-----------|----------|-----------|------|
| Aldosterone antagonists | 226 (28%) | 28 (21%) | 198 (30%) | 0.07 |
| Angiotensin-neprilysin inhibitor | 25 (3%) | 1 (1%) | 24 (4%) | 0.16 |

Plus-minus values are given as mean \pm standard deviation; ACEI — angiotensin converting enzyme inhibitors;

AV — atrioventricular; CIED — cardiovascular implantable electronic device; IQR — interquartile range;

NYHA — New York Heart Association

^aB-type natriuretic peptide was available in only 702 of 802 patients (88%)

^bOther cardiac diseases include hypertrophic cardiomyopathy, cardiac sarcoidosis, cardiac amyloidosis, and tricuspid valve replacement

^cImplantable cardioverter-defibrillator without symptomatic bradyarrhythmia at implant

Table 2. Results of the multivariate analysis for pacing dependency in 802 study patients

| Clinical variable | OR (95% CI) ^a | P ^a |
|---|--------------------------|----------------|
| Left ventricular ejection fraction \leq 30% | 2.06 (1.03–4.15) | 0.04 |
| Brain natriuretic peptide >150 pg/mL | 2.12 (1.16–3.97) | 0.02 |
| Second- or third-degree AV block at implant | 19.9 (10.9– 8.5) | < 0.01 |
| Atrial fibrillation before implant | 2.15 (1.16–4.05) | 0.02 |
| Chronic kidney disease | 1.86 (1.08–3.26) | 0.03 |
| Implant duration > 5 years | 3.29 (1.96–5.64) | < 0.01 |

AV — atrioventricular; CI — confidence intervals; OR — odds ratio

^aAfter adjustment for potential confounding clinical variables as summarized in Table 1 including medication, implantable cardioverter defibrillator therapy and cardiac resynchronization therapy

Table 3. Subgroup analysis of 563 patients with permanent pacemaker.

| | All patients | Pacemaker dependency | | P |
|---|--------------|----------------------|--------------|--------|
| Clinical variable | N = 563 | Yes (n = 103) | No (n = 460) | |
| Age [years] | 76 \pm 12 | 77 \pm 12 | 76 \pm 12 | 0.57 |
| Male gender | 336 (60%) | 68 (66%) | 268 (58%) | 0.18 |
| Atrial fibrillation before implant | 194 (34%) | 30 (29%) | 164 (36%) | 0.25 |
| Left bundle branch block at implant | 71 (13%) | 11 (11%) | 60 (13%) | 0.51 |
| Chronic kidney disease | 230 (41%) | 55 (53%) | 175 (38%) | < 0.01 |
| Heart failure severity | | | | |
| Left ventricular ejection fraction \leq 30% | 60 (11%) | 18 (17%) | 42 (9%) | 0.02 |
| NYHA functional class III or IV | 195 (35%) | 53 (51%) | 142 (31%) | < 0.01 |

| | | | | |
|--|-----------|----------|-----------|--------|
| B-type natriuretic peptide >150 pg/mL ^a | 264 (54%) | 56 (68%) | 208 (51%) | < 0.01 |
| Underlying cardiac disease | | | | |
| Coronary artery disease | 201 (36%) | 37 (37%) | 164 (36%) | 0.05 |
| Nonischemic dilated cardiomyopathy | 26 (5%) | 8 (8%) | 18 (4%) | |
| Hypertensive heart disease | 169 (30%) | 35 (34%) | 134 (29%) | |
| Valvular heart disease | 88 (16%) | 16 (16%) | 72 (16%) | |
| Other cardiac diseases ^b | 5 (1%) | 3 (3%) | 2 (0.4%) | |
| No structural heart disease | 74 (13%) | 4 (4%) | 70 (15%) | |
| Previous cardiac surgery | | | | |
| Aortocoronary bypass grafting | 55 (10%) | 11 (11%) | 44 (10%) | 0.87 |
| Surgical aortic valve replacement | 20 (4%) | 4 (4%) | 16 (3%) | 0.84 |
| Mitral valve reconstruction or replacement | 12 (2%) | 1 (1%) | 11 (2%) | 0.37 |
| Transcatheter aortic valve replacement | 41 (7%) | 8 (8%) | 33 (7%) | 0.83 |
| Indication for pacemaker implantation | | | | |
| Sick sinus syndrome | 190 (34%) | 12 (12%) | 178 (39%) | < 0.01 |
| Second or third-degree AV block | 227 (40%) | 79 (77%) | 148 (32%) | |
| Atrial fibrillation with bradycardia | 119 (21%) | 12 (12%) | 107 (23%) | |
| Carotid sinus syndrome | 2 (0.4%) | 0 (0%) | 2 (0.4%) | |
| Cardiac resynchronisation ^b | 25 (4%) | 0 (0%) | 25 (5%) | |
| Implant duration > 5 years | 222 (39%) | 59 (57%) | 163 (35%) | < 0.01 |
| Medication | | | | |
| Beta-blockers | 331 (59%) | 59 (57%) | 272 (59%) | 0.47 |
| Amiodarone | 18 (3%) | 0 (0%) | 18 (4%) | 0.08 |
| Digitalis | 46 (8%) | 5 (5%) | 41 (9%) | 0.25 |
| ACEI | 278 (43%) | 58 (56%) | 220 (48%) | 0.15 |
| Angiotensin receptor blockers | 114 (20%) | 18 (17%) | 96 (21%) | 0.52 |
| Diuretics | 362 (64%) | 73 (71%) | 289 (63%) | 0.12 |
| Aldosterone antagonists | 89 (16%) | 12 (12%) | 77 (17%) | 0.26 |
| Angiotensin-neprilysin inhibitor | 9 (2%) | 1 (1%) | 8 (2%) | 0.89 |

Abbreviations as in Table 1.

^aB-type natriuretic peptide was available only in 467 of 539 patients (66%)

^bPatients with heart failure and left bundle branch block

Table 4. Subgroup analysis of 239 patients with implantable cardioverter-defibrillator.

| | All patients | Pacemaker dependency | | P |
|---|------------------|----------------------|-----------------|-------------|
| Clinical variable | N = 239 | Yes (n = 28) | No (n = 211) | |
| Age [years] | 68 ± 12 | 68 ± 12 | 68 ± 12 | 0.93 |
| Male gender | 185 (77%) | 21 (75%) | 164 (78%) | 0.81 |
| Atrial fibrillation before implant | 48 (20%) | 8 (29%) | 40 (19%) | 0.41 |
| Left bundle branch block at implant | 70 (29%) | 14 (50%) | 56 (25%) | 0.02 |
| Chronic kidney disease | 100 (42%) | 15 (54%) | 85 (40%) | 0.18 |
| Heart failure severity | | | | |
| Left ventricular ejection fraction ≤ 30% | 119 (50%) | 23 (82%) | 96 (45%) | < 0.01 |
| NYHA functional class III or IV | 125 (52%) | 21 (75%) | 104 (49%) | 0.01 |
| Brain natriuretic peptide >150 pg/mL ^a | 144 (61%) | 21 (78%) | 123 (59%) | < 0.01 |
| Underlying cardiac disease | | | | |
| Coronary artery disease | 112 (47%) | 8 (29%) | 104 (49%) | 0.03 |
| Nonischemic dilated cardiomyopathy | 93 (39%) | 18 (64%) | 75 (36%) | |
| Hypertensive heart disease | 11 (5%) | 0 (0%) | 11 (5%) | |
| Valvular heart disease | 13 (5%) | 1 (4%) | 12 (6%) | |
| Other cardiac diseases ^b | 8 (3%) | 1 (4%) | 7 (3%) | |
| No structural heart disease | 2 (1%) | 0 (0%) | 2 (1%) | |
| Previous cardiac surgery | | | | |
| Aortocoronary bypass grafting | 40 (17%) | 6 (21%) | 34 (16%) | 0.66 |
| Surgical aortic valve replacement | 9 (4%) | 0 (0%) | 9 (4%) | 0.27 |
| Mitral valve reconstruction or replacement | 3 (1%) | 0 (0%) | 3 (1%) | 1.00 |
| Transcatheter aortic-valve replacement | 2 (1%) | 1 (4%) | 1 (0.5%) | 0.56 |
| Indication for antibradycardia pacing at ICD implant | | | | |
| Sick sinus syndrome | 6 (3%) | 0 (0%) | 6 (3%) | <0.01 |
| Second or third-degree AV block | 20 (8%) | 16 (57%) | 4 (2%) | |
| Atrial fibrillation with bradycardia | 6 (3%) | 2 (7%) | 4 (2%) | |
| Cardiac resynchronization therapy ^b | 68 (28%) | 20 (71%) | 48 (23%) | |
| Implant duration > 5 years | 108 (45%) | 15 (54%) | 93 (44%) | 0.03 |
| Medication, | | | | |
| Beta-blockers | 208 (87%) | 26 (93%) | 182 (86%) | 0.49 |
| Amiodarone | 26 (11%) | 7 (25%) | 19 (9%) | 0.03 |
| Digitalis | 22 (9%) | 4 (14%) | 18 (9%) | 0.52 |

| | | | | |
|----------------------------------|-----------|----------|-----------|------|
| ACEI | 141 (59%) | 19 (68%) | 122 (58%) | 0.31 |
| Angiotensin receptor blockers | 57 (24%) | 7 (25%) | 50 (24%) | 0.88 |
| Diuretics | 187 (78%) | 27 (96%) | 160 (76%) | 0.03 |
| Aldosterone antagonists | 137 (57%) | 16 (57%) | 121 (57%) | 0.98 |
| Angiotensin-neprilysin inhibitor | 16 (7%) | 0 (0%) | 16 (8%) | 0.27 |

Abbreviations as in Table 1.

^aB-type natriuretic peptide was available in 235 of 239 patients (98%)

^bPatients with heart failure and left bundle branch block

Table 5. Prevalence of pacing-dependency in studies with at least 50 patients.

| Author | Year | Patients | ICD | Cardiac surgery | Follow-up [months] | Pacing-dependency | Intrinsic rhythm [bpm] ^a |
|-----------------------|------|----------|------|-----------------|--------------------|-------------------|-------------------------------------|
| Glikson et al. [3] | 1997 | 86 | 0% | 100% | 41 (median) | 51 (59%) | < 50 |
| Tang et al. [4] | 2001 | 2244 | 0% | NA | 2 to 8 | 484 (22%) | < 40 |
| Nagatomo et al. [5] | 2004 | 518 | 0% | NA | 44 ± 32 | 23 (4%) | < 30 |
| Lelakowski et al. [6] | 2007 | 3638 | 0% | NA | 58 ± 22 | 76 (2%) | < 30 |
| Onalan et al. [7] | 2008 | 102 | 0% | 100% | 48 (mean) | 21 (23%) | < 30 |
| Merin et al. [8] | 2009 | 58 | 0% | 100% | 72 ± 32 | 37 (63%) | < 40 |
| Raza et al. [9] | 2011 | 90 | 0% | 100% | 67 ± 50 | 36 (40%) | < 40 |
| Rene et al. [10] | 2013 | 98 | 0% | 100% | 43 ± 41 | 44 (45%) | < 30 |
| Sood et al. [11] | 2013 | 1058 | 100% | NA | 50 ± 41 | 142 (13%) | < 40 ^b |
| Present study | 2019 | 802 | 30% | 30% | 67 ± 70 | 131 (16%) | < 30 |

NA — data not available

^aIntrinsic rhythm used to define pacemaker dependency

^bIntrinsic rhythm < 40 bpm or < 50 bpm with symptoms

Figure 1. Electrocardiogram recordings with a paper speed of 25 mm/s showing typical examples of ventricular asystole following transient inhibition of pacing; **A.** Ventricular asystole due to third degree atrioventricular (AV) block without ventricular escape rhythm in a patient with permanent atrial fibrillation; **B.** Ventricular asystole due to sinus arrest without escape rhythm in a patient with sinus node disease; **C.** Ventricular asystole due to third degree AV block without ventricular escape rhythm in a patient with second degree AV block type Mobitz at the time of pacemaker implant.

Figure 1A

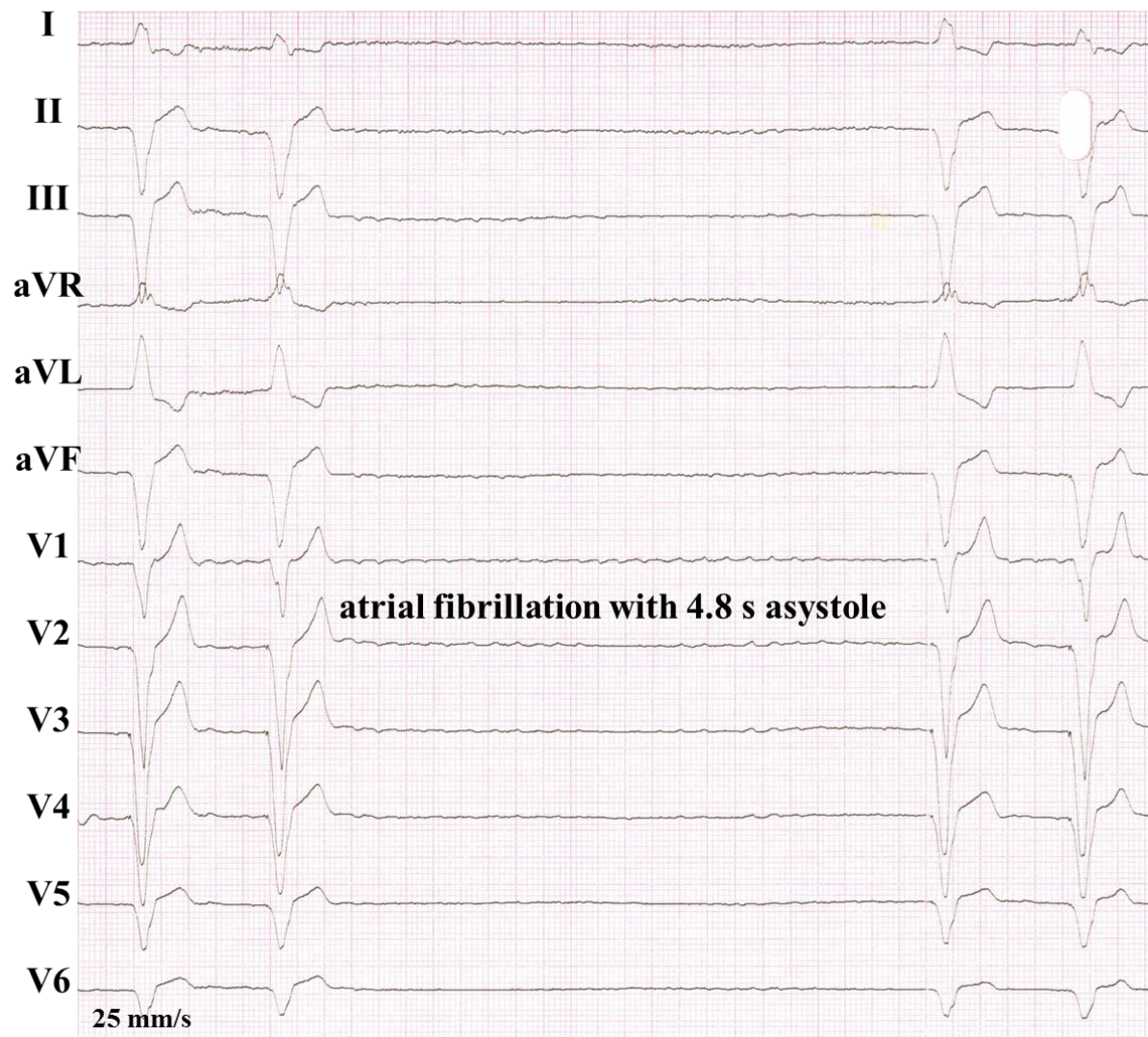


Figure 1B

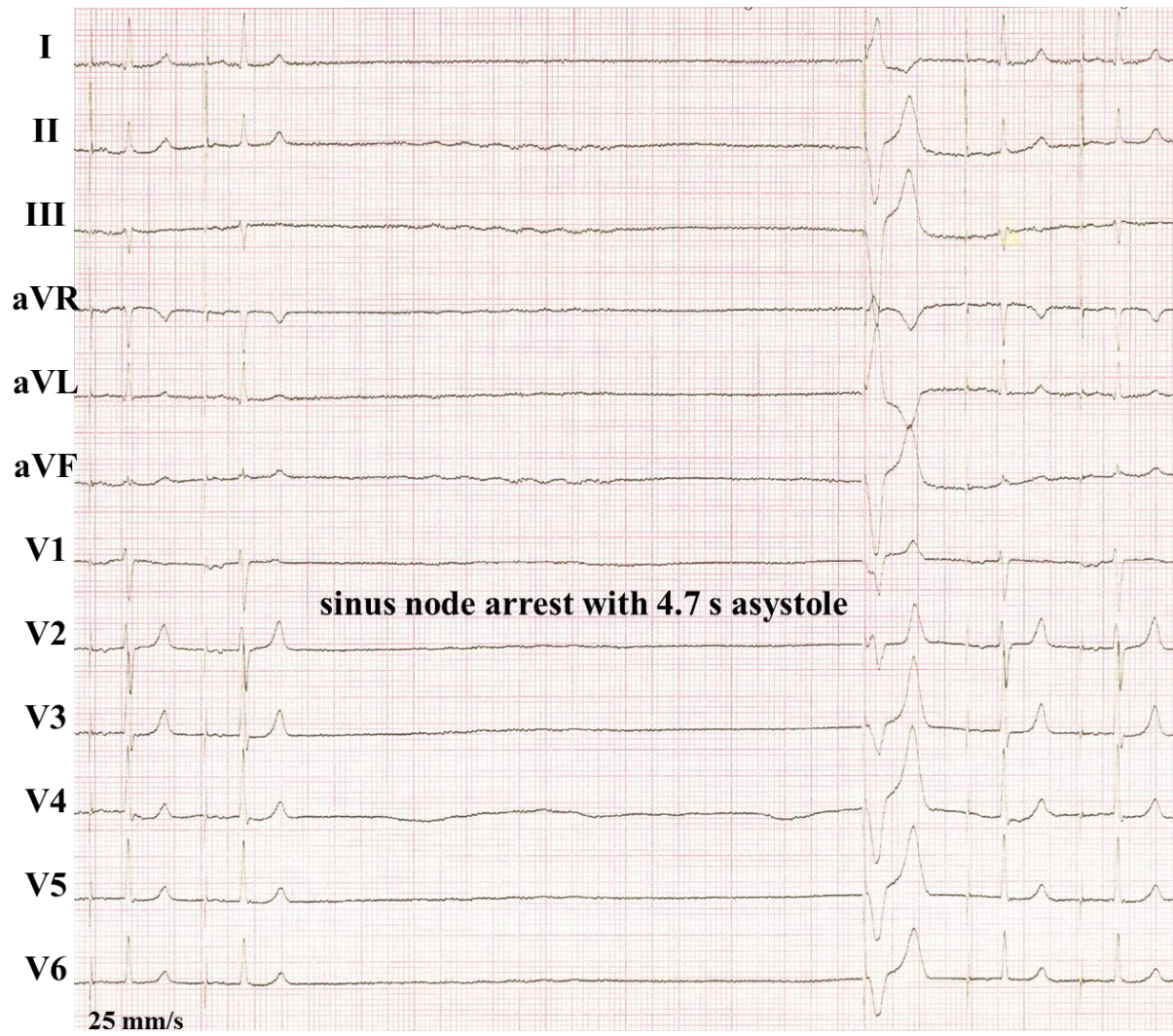


Figure 1C

